

With the Author's Compl

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NITRITE OF AMYL IN ANGINA
PECTORIS.

BY

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Nitrite of Amyl in Angina Pectoris. By T. LAUDER BRUNTON, M.D. Communicated by J. BURDON SANDERSON, M.D. *Read February 11, 1870.*

WILLIAM H., æt. 26; formerly a blacksmith, now a toll-keeper; admitted to Ward I., Royal Infirmary, Edinburgh, December 7, 1866.

Antecedent History.—Patient was strong and healthy till his tenth year, when he was confined to bed for six months by a severe attack of rheumatism. During the next twelve years he had four other less severe attacks, and after recovering from the last of these his feet began to swell during the day.

In April 1866, he had a seventh attack, which lasted for a month, and six weeks after it was over he noticed an unusual palpitation of his heart, for which he entered the infirmary, and remained there three weeks, but left unrelieved. The palpitation gradually increased till he felt it along the line of the carotids as high up as the ears; and in November last he began to feel besides a dull heavy pain about the left nipple. At first this came on every three days, usually during the night, and lasted half an hour. During the day he felt little inconvenience from the palpitation, unless he exerted himself.

On admission the pain was no longer confined to the region of the left nipple, but was worst along the right border of the sternum, and extended up to the right arm. This pain was more severe if he walked about much, otherwise he felt well. Professor MacLagan had charge of the clinical wards at this time, and the patient was treated for six weeks with tincture of aconite, and then with tincture of digitalis; but under these remedies the pulse became intermittent, and the pain was not relieved by either, and rather aggravated by digitalis. They were therefore discontinued, the digitalis being stopped on January 31. Their employment wet cupping over the cardiac region the extent of $\frac{3}{4}$ in. temporarily relieved the pain.

February 1st, Professor MacLagan's term of office having expired, Professor Bennett took charge of the clinical wards.

On February 5th, the patient began to complain of pain in the back, neck, head, thighs, and elbow-joints; he had no appetite, was perspiring profusely, and his pulse was 116, full and strong. Next day the pain was most severe in the shoulders, back, hip, and knee-joints.

On the 8th he was examined by Professor Bennett and the clinical class, and the following was found to be the condition of his circulatory system:—Apex beat $2\frac{1}{4}$ inches below and $2\frac{1}{2}$ inches to the outside of the left nipple. On palpation, pulsation is felt over the whole left front and side of thorax, most strongly between the fourth and sixth ribs, and faintly over the supraclavicular region.

Cardiac dulness commences at the middle line of the sternum and extends laterally outwards for 5 inches.

A loud, double, blowing sound is heard over the whole of the cardiac region, but is loudest at the base. Over the right sterno-clavicular articulation a single blowing is heard. Pulse 104, strong and jerking. The respiratory system was normal, the skin covered with an acid sweat, the tongue furred, no appetite, urine high-coloured and slightly albuminous. The pain in the joints continued along with pain in the neck in the line of the carotids, but the pain in the cardiac region was absent.

On the 11th the pulse fell to 80, and the pain in the joints diminished, but the patient was still troubled by pain in the left ear, and along the line of the carotids, with violent pulsation in them at night.

On the 18th the rheumatic pains in the joints and shoulders had entirely disappeared, but the pain in the cardiac region came on during the night.

On the 19th four ounces of blood were taken from the arm, with immediate relief to the pain and violent pulsation, and the pain over the heart, which usually came on at 3 A.M., was much less on the ensuing night.

25.—Patient's appetite remains unimpaired by the pain, and he takes all his food, consisting of steak diet, beef-tea, potatoes, and bread. *Pil. colocynth. c. hyoscy.* every other night. Ordered *tinct. lobeliae*, 20 drops three times a day.

27.—The pain continued to come on during the night. $\bar{\text{z}}$ iv. of blood were taken from the arm at 10 P.M. An hour after patient went to sleep, had a good night, and the pain did not come on.

March 3.—Pain felt at 11 P.M. in breast and ears. A poultice applied over the breast gave some relief.

6.—Pain severe at 3 A.M., lasting for about 1 hour. At 9 A.M. $\bar{5}$ ij. of blood were taken from the arm. At 10 A.M. pulse 76, not so forcible as yesterday.

7.—No pain during the night.

8.—Pain came on as usual during the night. Tinct. lobeliae to be stopped.

9.— $\bar{5}$ j. of brandy to be taken when the pain comes on.

10.—The pain came on in the night and was not relieved by the brandy.

12.—The pain came on as usual at 3 A.M. A few drops of nitrite of amyl were put on a towel and inhaled by the patient. The primary effect noticed was a suffusion of the face, and the patient felt a glow over his face and chest. The pain disappeared almost simultaneously with the occurrence of these phenomena, but returned in 3 minutes. He then inhaled 5 drops more; the pain again disappeared and did not return.

16.—The pain has recurred each night and been relieved by the inhalation of 10 drops of nitrite of amyl. Last night it came on about 10.30 P.M., the same in position and character as before. On the patient's taking 10 drops of nitrite of amyl in $\bar{5}$ ss. of brandy, the pain went away, but returned in 3 minutes; 5 drops were then inhaled from a towel, and the pain disappeared. He went to sleep in an hour and slept till 3 A.M., when he was awaked by a return of the pain. He drank 10 drops in a little brandy, but, no effect following, he inhaled a few drops. The pain disappeared and did not return.

17.—Pain came on at 1 A.M.; 10 drops were given internally. The pain was relieved, but returned in a few minutes; 10 drops were then inhaled. The pain disappeared and did not return.

Dr. Bennett, thinking the relief of pain by the amyl might be due to anæsthesia, ordered chloroform to be tried during the attack.

18.—About 2 A.M. the pain came on as usual, and chloroform was inhaled by the patient. He was only partly put under it, and as soon as he again became completely conscious the pain was found to be present as before; 6 drops of nitrite of amyl were then given by inhalation. The pain disappeared and did not return.

March 25.—The pain came on at 1.58 A.M., but was not

very bad. While it was present the pulse was 100, respirations 32. After amyl was given, but the pain not quite gone, the pulse was 130, fell with the disappearance of the pain to 100, and twelve minutes after was 80, and respirations 24.

April 6.—The pain had come on about 2.35 A.M., and the patient was relieved by a whiff of amyl, but the pain began to return at the end of the sternum, right ear, and right shoulder. The chest was auscultated, but no abnormal sounds could be detected to indicate any coincident spasm of the bronchial tubes.

April 10.—Patient continues to have the pain every night, and instead of inhaling the nitrite of amyl from a cloth, does so from the bottle. Two or three inhalations usually suffice to relieve the pain. Up to the 8th he used pure nitrite made by Dr. Gamgee, but this being finished, he then began to use some made by Macfarlan & Co.; but the smell of it was not so agreeable, and it sometimes occasioned headache, which the pure amyl never did.

April 14.—The pain has been coming on several times during the night, is most intense at a spot 2 in. inside of the right nipple, remains there after it has gone from the rest of the chest, and is only removed by repeated inhalation. Last night it came on three times and was relieved by amyl each time, but five or six inhalations were required. To-day at 11 A.M. $\frac{3}{4}$ iv. of blood were taken from the patient's arm, and he was ordered potass. iod. gr. viij. three times a day.

17.—Pain came on during the night and continued uninterruptedly for one hour and a half. By Dr. Bennett's order no amyl was taken, in order to determine whether the relief of the pain was due to it or to some change in the symptoms independent of it. Three dry cups were applied over the cardiac region. They did not relieve the pain.

18.—No pain during the night. No amyl taken.

19.—Very little pain, lasting half an hour. Took no amyl.

May 9.—Has had the spasmodic pain every night. Last night it came on five times, at intervals of about an hour, and was in each case relieved by inhalation.

15.—Pain has been rather less during the past two nights. Attention was called to-day to purpuric spots upon both legs, which the patient had noticed some days previously. Gums neither swollen nor tender. His diet for some time past has been beef-steak and potatoes, with porridge and milk for

breakfast. The use of iodide of potassium to be suspended.

17.—Pain came on severely in the chest a little after midnight. It was worst 2 inches inside of the right nipple.

Tracing 1.—0h. 22' A.M. Pulse 104 small, resp. 36. There is a thrill to be heard and felt with the second sound at the apex.

22' 40" 13 drops inhaled from a cloth.

Tracing 2.—0h. 24' 0" The lever of the sphygmograph has risen very much. The pain has gone, except at a point 2 inches inside of right nipple.

25' 30" 5 drops more given; pulse 112.

0h. 28' 0" Pain almost gone; patient now inhaled from the bottle; pulse 100.

Tracing 3.—0h. 34' 0" Pain has been gone for 4 minutes, but at 37' it began to return inside the right nipple, and a little more was inhaled.

0h. 40' 0" Pain quite gone; pulse 92; resp. 28.

Tracing 4.—0h. 47' 0" Pain did not return.

In these tracings, like the others, the patient's position was unchanged, and neither the band nor pressure screw of sphygmograph was touched.

18.—Pain came on three times last night and was very severe. He has had it during the day three times. The purpuric spots on the legs are much paler. To recommence iodide of potassium.

21.—The purpuric spots have reappeared on both legs. To stop the pot. iod. He had pain last night, but none during the day.

24.—Bled to $\bar{\text{z}}$ iv. on account of general uneasiness and powerful pulsations of the heart. The bleeding was immediately followed by a sense of relief.

28.—The pain has only been absent one night since the bleeding, but it has been much less severe than before it. The sphygmograph was fixed to his arm to-night in order to take a normal tracing for comparison with one to be taken during the attack. This had scarcely been done when the pain unexpectedly came on. The tracing, though unfortunately very imperfect, shows the diminished volume and

increased tension of the pulse. In 2 the pain was severe, and 3 was taken after inhalation of amyl.

June 1.—Condition remains the same, spasmodic pain in the cardiac region occurring every night, but not severe, and easily relieved by a few inhalations of nitrite of amyl. Patient wished to resume his former occupation of toll-keeper, and was to-day discharged at his own request. Recommended to have occasional small bleedings.

Remarks.—In this case of Dr. Bennett's, which by his kind permission I now publish, we have a history of numerous attacks of rheumatic fever, followed by cardiac lesion, which was accompanied by palpitation of the heart, throbbing in the carotids extending as high as the ears, and a spasmodic pain in the chest. This pain was sometimes most severe near the left nipple, and sometimes at the right border of the sternum, but extended over the whole cardiac region, and shot up to the right ear and down the right arm. It used to come on suddenly during the night, generally between midnight and 3 A.M., was accompanied by little or no feeling of dyspnoea, and was somewhat relieved by the patient's sitting up. It generally came on every third night at first, but latterly every night, and was worse when the patient had used much exertion during the day. It was not relieved by tincture of aconite, tincture of *Lobelia inflata*, brandy, or dry cupping over the cardiac region. It was made worse rather than better by tincture of digitalis. It was temporarily relieved by chloroform, but whenever the stupefying effect passed off the pain was as bad as before. It was somewhat relieved by warm poultices to the chest, and was generally absent for one night after a small bleeding, either from the arm or by cupping the chest. Under the use of iodide of potassium the attacks became less frequent, but purpuric spots appeared on the limbs, and each attack was at once relieved by the inhalation of nitrite of amyl. During an attack of rheumatic fever it disappeared completely, again returning with the departure of the rheumatic pains.

Angina pectoris is defined by Dr. Walsh as a paroxysmal neurosis, in which the heart is essentially concerned, and he divides it into pseudo and true angina, which differ mainly in the intensity of the symptoms. Friedreich and others divide it into functional and organic, according as it is accompanied by cardiac lesion or not. From the absence of a

sense of impending death, the present case might be reckoned as one of pseudo angina, but in the intensity of the pain and the manner of its radiation it more closely resembles true angina. As cardiac lesion was present, it belongs to the class organic angina.

Various opinions have been advanced as to the pathology of this disease, some saying it is a mere brachio-thoracic neuralgia, but most holding that it is a neuralgic affection of the cardiac plexus. Some are of opinion that it is associated with cramp of the heart, others with weakness of that organ.

Eichwald* thinks that there is not only weakness of the heart, but a mechanical impediment to its action, produced by irritation of its regulating nerves, and that the pain is caused by unavailing efforts to overcome this obstacle. Nothnagel† states that during angina there is pallor and coldness of the extremities, small pulse, and other symptoms of a cramp-like contraction of the systemic arteries, and that the spasm is relieved by remedies which cause their relaxation, such as warm baths and friction.

It is quite possible that the pathology of all cases classed under angina pectoris is not the same, and that the differences of opinion are not due merely to the want of exact methods of observation. What the nature of the attack was in the present case may be learned to some extent from an examination of the sphygmographic tracings, which were begun by direction of Dr. Maclagan, and continued during the time the case was in the wards under the care of Dr. Bennett. In taking these tracings, the instrument, which was one of Marey's, without any means of estimating the pressure employed, was applied to the arm above the end of the radius, as it was found to cause pain when applied over the bone for any length of time. The amplitude of the curve thus obtained is greater, and it did not occur to me till after studying the physiology of the circulation under Professor Ludwig, that in such cases as the present, where sudden changes occur in the vessels, I was increasing the fallacy which the variation in the height of the lever from turgescence of the tissues produces, and which may be confounded with a rise from increased tension in the vessels. Except where marked otherwise, the tracings were all taken with the patient in a recumbent position, and neither the

* Würzburg. med. Zeitschr. iv. 249; Cblt. f. med. Wiss. i. 877.

† Deut. Arch. f. klin. Med. iii. 309; Cblt. med. Wiss. v. 715.

cord by which the instrument was attached to the arm, nor the screw regulating the pressure, was touched during the observation.

The case excited considerable interest, and was carefully observed and commented on by Professor Bennett to the clinical class, and the cardiac lesion was diagnosed by him from the physical signs to be aortic obstruction and regurgitation, with dilatation of the aorta, but no sacculated aneurism.

The tracings confirm this diagnosis, showing in a typical manner the abrupt ascent, terminating in a hook, of each wave, characteristic of the unfilled arteries, which aortic regurgitation produces, and the long and rounded apex of aortic obstruction. There is, however, a marked difference between the tracings from the two radials, the ascent of the wave being more abrupt, the top flatter, and the descent distinctly dichrotic in the right, while in the left the ascent is less abrupt, as shown by the smaller hook at the top; the maximum height is not attained till near the end of the systole, and there is generally little or no dichrotism in the descent. This might be due to aneurism; but there were no physical signs to show its presence, and in the absence of a post-mortem examination, or experiment with a schema, hypotheses as to the cause of difference are of little value.

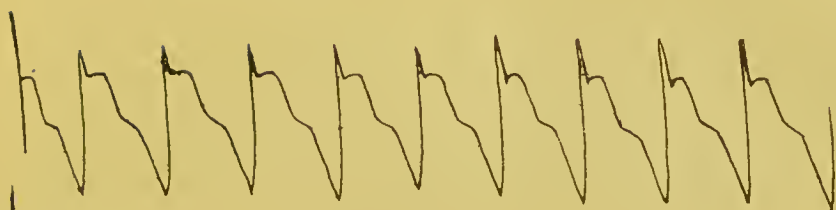
The tracings taken during an attack were chiefly from the right radial. The only one I got while the pain was actually coming on is unfortunately an imperfect one (No. 1, May 28). From this tracing, and from those taken when the pain was becoming worse (Nos. 1 and 2 of May 17), it will be seen that as the pain increased the curve became lower, both the ascent and descent more gradual, and the dichrotism disappeared. This form of curve clearly indicates that the arterial tension is much increased, and this increase can, I think, be due only to contraction of the small systemic vessels, so sudden and so great as well to deserve the name of spasmodic. As I have stated in a former paper,* this increased tension led me to suggest nitrite of amyl to relieve the spasm.† The rapidity with which this increase in tension takes place is shown by the great change which the form of the pulse has undergone in tracing 1, May 28, during the short time occupied in re-inking the pen. It would seem from tracings 3 and 4 of the plate that the tension in the right radial was

* 'Lancet,' July 27, 1867.

† Dr. Bennett, on being informed of the successful result of the first experiment, ordered the inhalation to be continued.

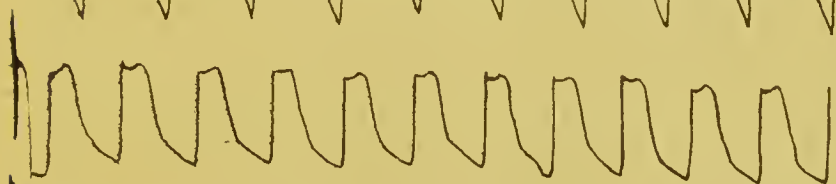
TRACINGS OF THE PULSE

IN ANGINA PECTORIS

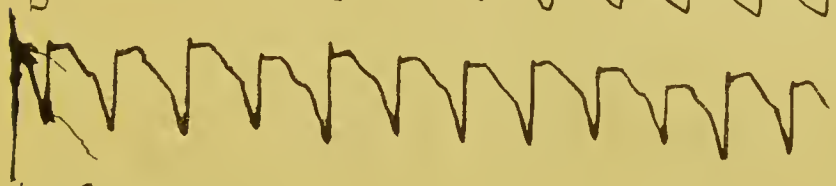


NORMAL PULSE

Right radial

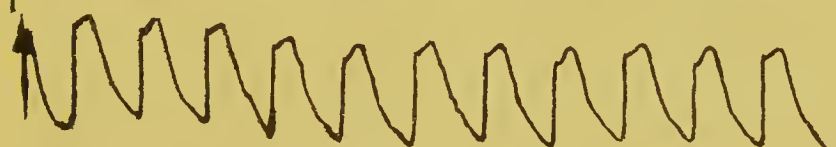


Left radial.



DURING ANGINA

Right radial.



Left radial.



MAY 17TH

1. Pain severe.

2. Pain gone except
near the nipple



3. Pain quite gone but
afterwards returned.

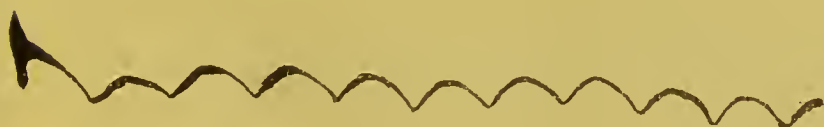


4. Pain gone and
did not return.

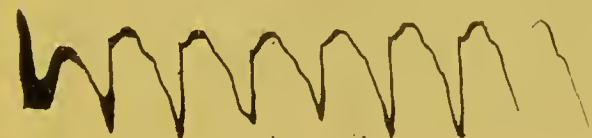


MAY 28TH

1. Pain coming on



2. Pain severe



3. Pain relieved by
Amyl.

raised more than in the left, and farther experiments with simultaneous tracings are necessary to decide whether the spasm extends to all systemic vessels or to all alike.

At the same time that the tension increases the pulse becomes somewhat quicker, which shows that there is some disturbance of the regulating apparatus of the heart, as normally the increased tension acting on the roots of the vagus should slow the pulse. It has been suggested to me (by Professor Ludwig) that the pain in the heart may be due to irritation of its sensory nerves by the great pressure of the blood, and that in the right arm and neck may be due to the same cause acting on the arteries, those of the right side being possibly contracted more than the left. Whenever the tension was lowered by nitrite of amyl the pain disappeared from the greater part of the cardiac region, the neck, and the arm, but sometimes remained persistent at a point about two inches to the inside of the right nipple. This I think indicates that the tension in the right ventricle was not yet relieved, and the small volume of the pulse (see tracing 3, May 17) seems to show that the amount of blood passing through the small pulmonary vessels at each systole was small, probably from contraction of their lumen. So long as this condition remained the pain was almost certain to return. It is possible that the right ventricle might not be able to empty itself completely at each systole, was therefore quickly refilled, and consequently contracted frequently, forcing the left ventricle to contract with it, and producing the rapid pulse with small volume seen in tracing 3 of May 17. The influence of the small vessels of the lungs over the circulation, though in all probability of extreme importance, is a subject of which we know as yet almost nothing.

The question whether the contractile power of either ventricle is lessened during the attack is one which cannot be decided with certainty from the present tracings. Digitalis, which has been recommended on the supposition that the heart is weak during the attack, proved productive in this case of more harm than good, contracting as it does the small vessels.

We may, I think, conclude that the attack in the present case consisted in a spasmodic contraction of some, if not all, of the small systemic, and probably of the pulmonary vessels, causing great increase in the blood-pressure in both sides of the heart; that this was probably due to a derangement of

> Such as is found in animals after division of the

the vaso-motor system, and accompanied by a derangement of the cardiac regulating apparatus, producing quickened instead of slowed pulsation; that the pain was not originally in the nerves composing the cardiac plexus, but produced by the pressure of the blood on those of the heart and arteries; and, from the alternation of the attacks with rheumatic pains in other parts of the body, that they were of rheumatic origin.

